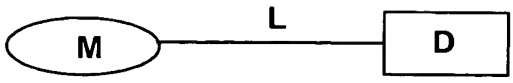
CLAIMS

1. A compound of Formula **I**:



I

wherein

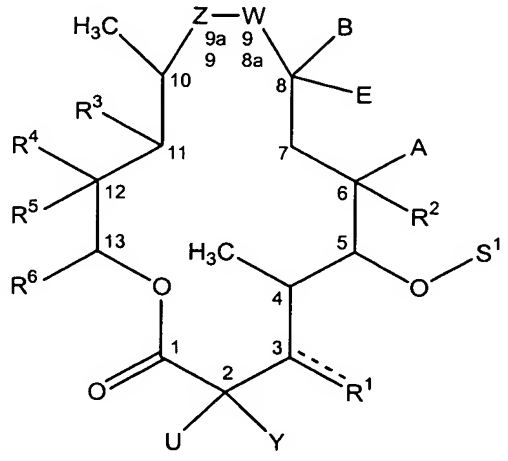
M represents a macrolide subunit;

D represents a nonsteroidal subunit;

L is a linker molecule to which each of **M** and **D** are covalently linked; and

pharmaceutically acceptable salts and solvates thereof and individual diastereoisomers thereof.

2. A compound according to claim 1 wherein **M** represents a group of Formula **II**:



II

wherein:

Z and W independently are: $>C=O$, $>CH_2$, $>CH\text{-}NR_tR_s$, $>N\text{-}R_N$ or $>C=N\text{-}R_M$ or a bond wherein:

R_t and R_s independently are hydrogen or alkyl;

R_M is hydroxy, alkoxy, substituted alkoxy or OR^p;

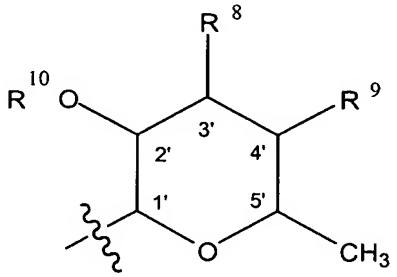
R_N is hydrogen, R^p, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or -C(X)-NR_tR_s; wherein X is $=O$ or $=S$;

provided that Z and W cannot both simultaneously be, $>C=O$, $>CH_2$, $>CH\text{-}NR_tR_s$, $>N\text{-}R_N$ or $>C=N\text{-}R_M$ or a bond,

U and Y independently are hydrogen, halogen, alkyl, or hydroxyalkyl;

R^1 is hydroxy, OR^p, -O-S^2 group or an $=O$;

S^1 is a sugar moiety of formula:



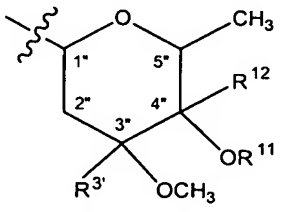
wherein

R^8 and R^9 are both hydrogen or together form a bond, or R^9 is hydrogen and R^8 is $-N(CH_3)R^y$, wherein

R^y is R^p, R^z or $-C(O)R^z$ wherein R^z is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with C_2-C_7-alkyl, C_2-C_7-alkenyl, C_2-C_7-alkynyl, aryl or heteroaryl

R^{10} is hydrogen or R^p;

S^2 is a sugar moiety of formula :



wherein:

$R^{3'}$ is hydrogen or methyl;

R^{11} is hydrogen, R^p or O-R^{11} is a group that with R^{12} and with C/4" carbon atom forms a $>C=O$ or epoxy group;

R^{12} is hydrogen or a group that with O-R^{11} group and with C/4" carbon atom forms a $>C=O$ or epoxy group;

R^2 is hydrogen, hydroxy, OR^p or alkoxy

A is hydrogen or methyl;

B is methyl or epoxy;

E is hydrogen or halogen;

R^3 is hydroxy, OR^p, alkoxy or R^3 is a group that with R^5 and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate; or if W or Z is $>N\text{-}R_N$ R^3 is a group that with W or Z forms a cyclic carbamate;

R^4 is C_1-C_4 alkyl;

R^5 is hydrogen, hydroxy, OR^p , C_1-C_4-alkoxy, or a group that with R^3 and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate;

R^6 is hydrogen or C_1-C_4-alkyl;

wherein **M** has a linkage site through which it is linked to **D** *via* linking group **L**; provided that the linkage site being at one or more of the following:

a) any reactive hydroxy, nitrogen, or epoxy group located on S^1, S^2, or an aglycone oxygen if S^1 or/and S^2 is cleaved off;

b) a reactive $>N\text{-}R_N$ or $-NR_tR_s$ or $=O$ group located on Z or W;

c) a reactive hydroxy group located at any one of R^1, R^2, R^3, and R^5;

d) any other group that can be first derivatized to a hydroxy or $-NR_tR_s$ group and

R^p is hydroxyl or amino protective group.

3. A compound according to claim 1 wherein **L** represents a group of Formula **IV**:

$$X^1\text{-}(CH_2)_m\text{-}Q\text{-}(CH_2)_n\text{-}X^2$$

IV

wherein

X^1 is selected from: $-CH_2-$, -C(O)-, OC(O)-, N-O- or -OC(O)NH-, -C(O)NH-;

X^2 is -NH- or -NHC(O)-, -OC(O)-, -C(O)-, -O or $-CH_2-$;

Q is -NH- or $-CH_2-$, or absent;

wherein each $-CH_2-$ or –NH- group may be optionally substituted by C_1-C_7-alkyl, C_2-C_7-alkenyl, C_2-C_7-alkynyl, $C(O)R^x$, $C(O)OR^x$, $C(O)NHR^x$ wherein R^x may be C_1-C_7-alkyl, aryl or heteroaryl;

the symbols m and n independently are a whole number from 0 to 4, with the proviso that if Q is NH, n cannot be 0.

4. A compound as claimed in claim 1 wherein **D** is derived from the NSAIDs selecting from: aceclofenac, acemetacin, acetaminophen, acetaminosalol, acetyl-salicylic acid, acetyl-salicylic-2-amino-4-picoline-acid, 5-aminoacetylsalicylic acid, alclofenac, aminoprofen, amfenac, ampyrone, ampiroxicam, anileridine, bendazac, benoxaprofen, bermoprofen, α-bisabolol, bromfenac, 5-bromosalicylic acid acetate, bromosaligenin, bucloxic acid, butibufen, carprofen, celexocib, chromoglycate, cinmetacin, clindanac, clopirac, sodium diclofenac, diflunisal, ditazol, droxicam, enfenamic acid, etodolac, etofenamate, felbinac, fenbufen, fenclozic acid, fendosal, fenoprofen, fentiazac, fepradinol, flufenac, flufenamic acid, flunixin, flunoxaprofen, flurbiprofen, glutametacin, glycol salicylate, ibufenac, ibuprofen, ibuproxam, indomethacin, indoprofen, isofezolac, isoxepac, isoxicam, ketoprofen, ketorolac, lornoxicam, loxoprofen, meclofenamic acid, mefenamic acid, meloxicam, mesalamine, metiazinic acid, mofezolac, montelukast, nabumetone, naproxen, niflumic acid, nimesulide, olsalazine, oxaceprol, oxaprozin, oxyphenbutazone, paracetamol, parsalmide, perisoxal, phenyl-acethyl-salicylate, phenylbutazone, phenylsalicylate, pyrazolac, piroxicam, pirprofen, pranoprofen, protizinic acid, reserveratol, salacetamide, salicylamide, salicylamide-O-acetyl acid, salicylsulphuric acid, salicin, salicylamide, salsalate, sulindac, suprofen, suxibutazone, tamoxifen, tenoxicam, tiaprofenic acid, tiaramide, ticlopridine, tinoridine, tolfenamic acid,

tolmetin, tropesin, xenbucin, ximoprofen, zaltoprofen, zomepirac, tomoxiprol, zafirlukast and cyclosporin.

5. A compound according to claim 2 wherein Z and W together are: $-N(CH_3)-CH_2-$, $-NH-CH_2-$, $-CH_2-NH-$, -C(O)-NH- or –NH-C(O)-;

A and B are methyl;

E is hydrogen;

R^2 is hydroxy or methoxy;

S^1 represents desosamine sugar wherein R^8 is selected from: hydrogen, methyl, amino, C_1-C_6 alkylamino or C_1-C_6 dialkylamino;

R^9 and R^{10} are hydrogen;

R^1 is hydroxy or the O-S^2 group wherein the S^2 represents a cladinose sugar wherein:

R^{11} is hydrogen, or O-R^{11} is a group that with R^{12} and with C/4" carbon atom forms a >C=O or epoxy group; R^{12} is hydrogen or a group that with O-R^{11} and with C/4" carbon atom forms a >C=O or epoxy group;

R^{13} is methyl;

U is hydrogen

Y is methyl;

R_6 is hydroxy, methyl or ethyl;

R^5 is hydrogen, hydroxy, methoxy or a group that with R^3 and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate bridge;

R^3 is hydroxy or a group that forms a cyclic carbamate bridge with W or Z, or R^3 is a group that with R^5 and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate bridge;

R^4 is methyl;

provided that the linkage is through the nitrogen of Z at N/9a position or through the carbon of R^{12} or through the oxygen of R^{11} both at C/4"position of the S^2 sugar.

6. A compound according to claim 3 wherein

X^1 is $-CH_2-$ or -OC(O)-;

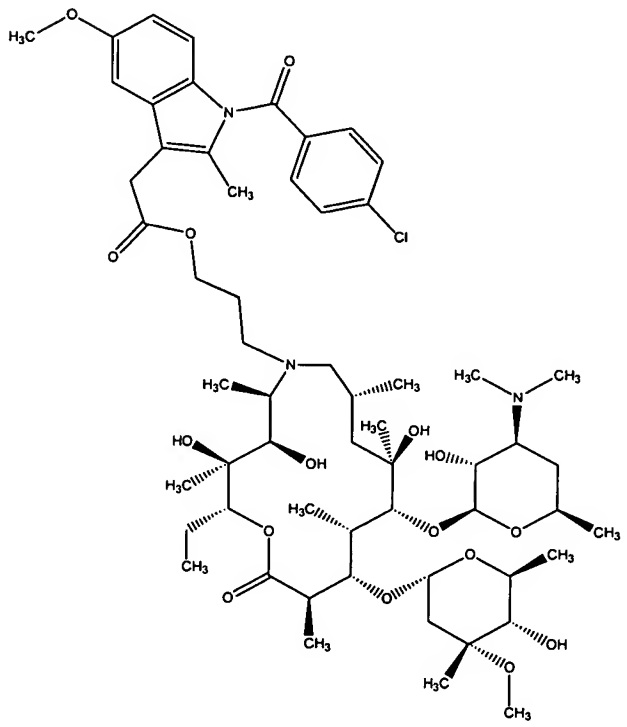
X^2 is -NHC(O)-;

Q is -NH- or absent.

7. A compound according to claim 4 wherein

D is derived from a NSAID selecting from: S-(+) - ibuprofen, indomethacin, flurbiprofen, naproxen, ketoprofen, acetyl salicylic acid, sulindac, etodolac, ketorolac, suprofen, flunixin, diclofenac sodium and tolmetin sodium.

8. A compound of the formula



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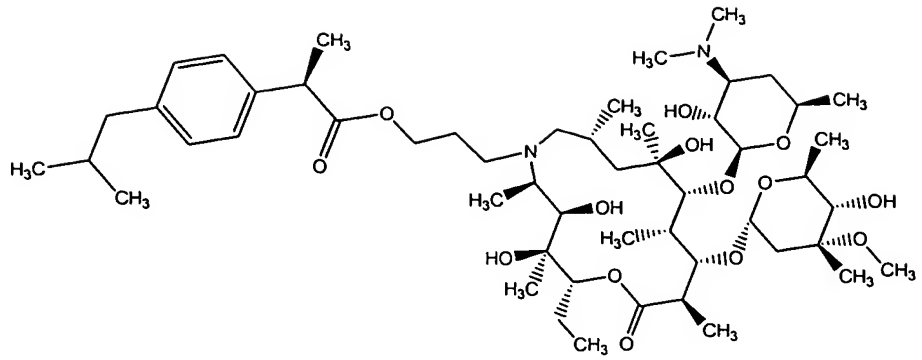

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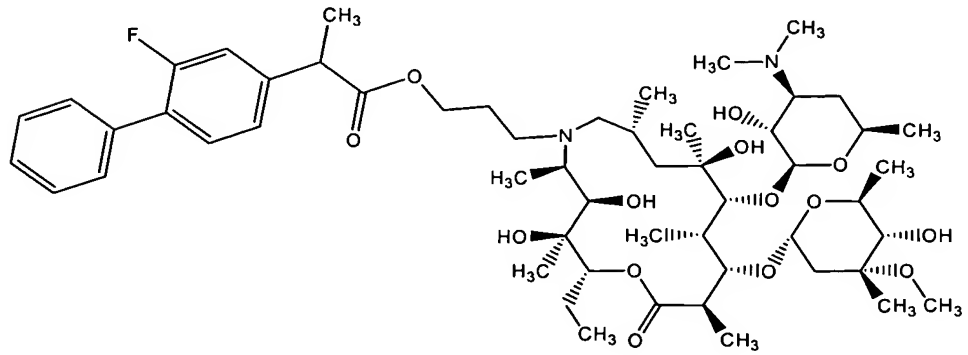

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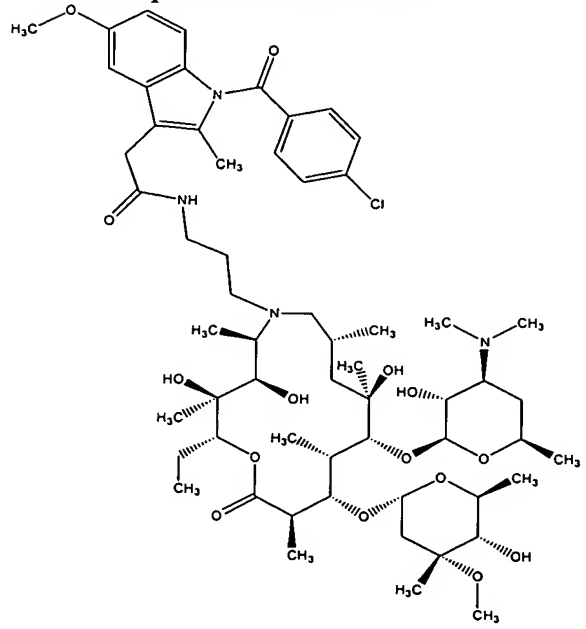

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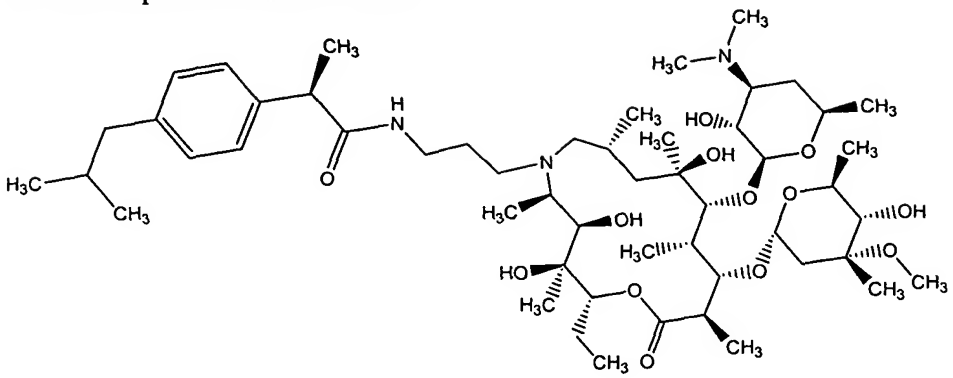

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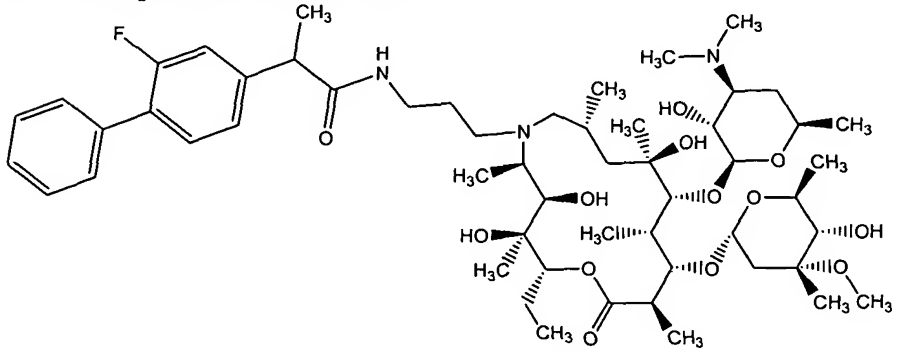

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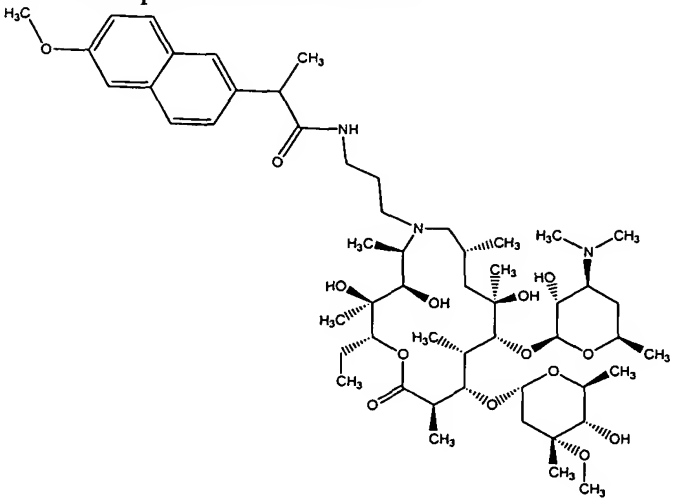

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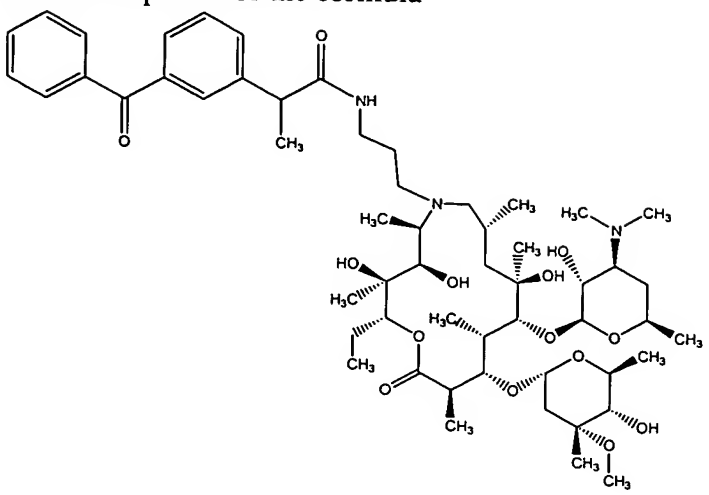

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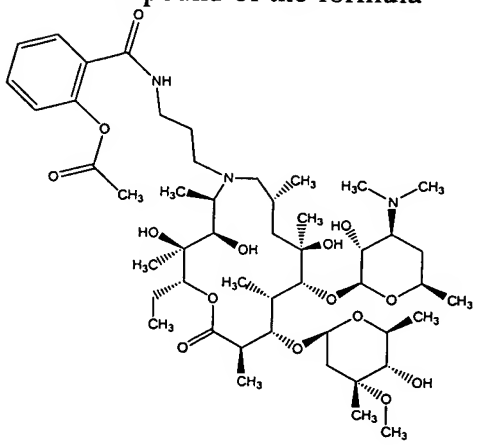

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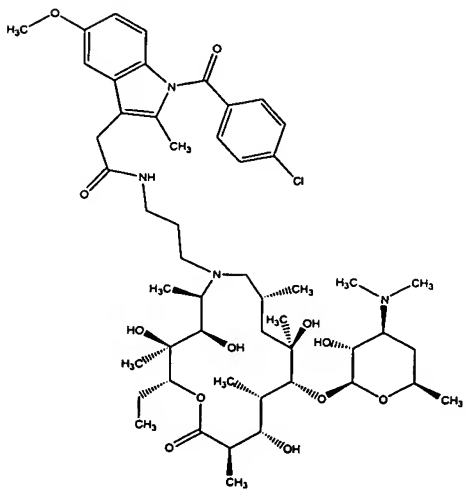

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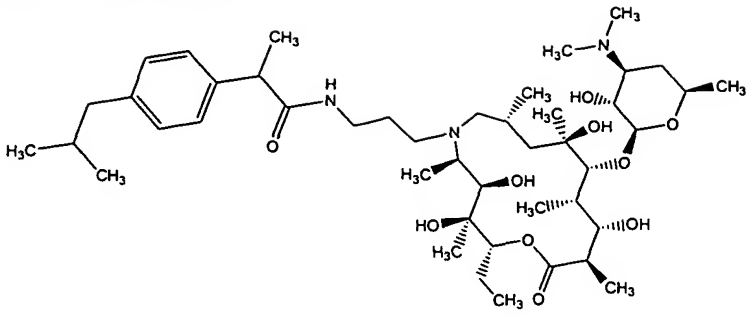

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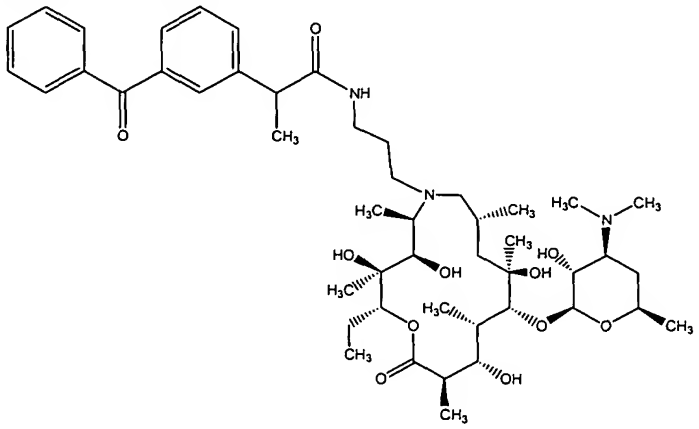

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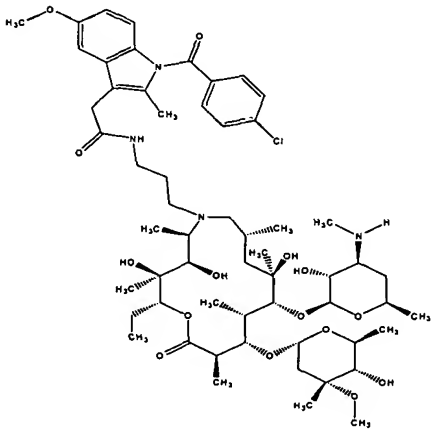

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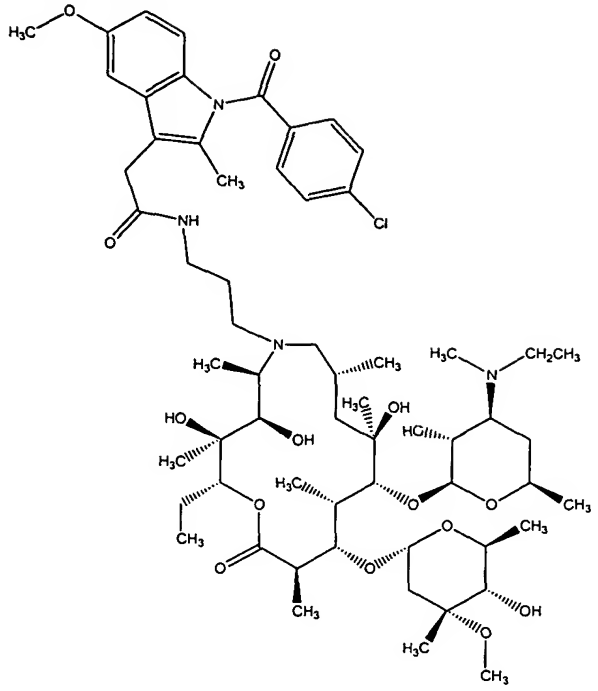

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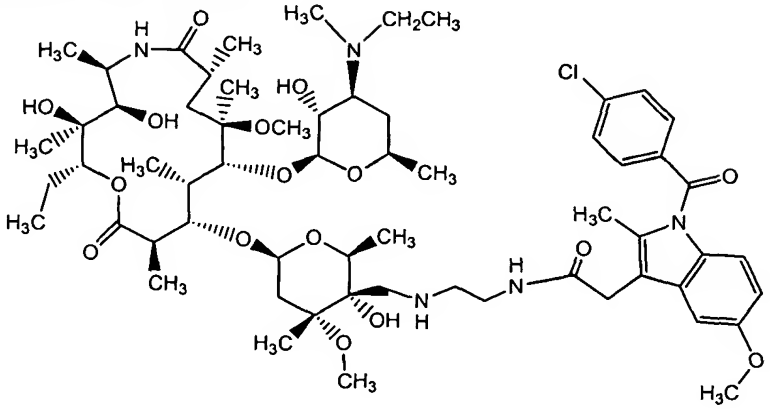

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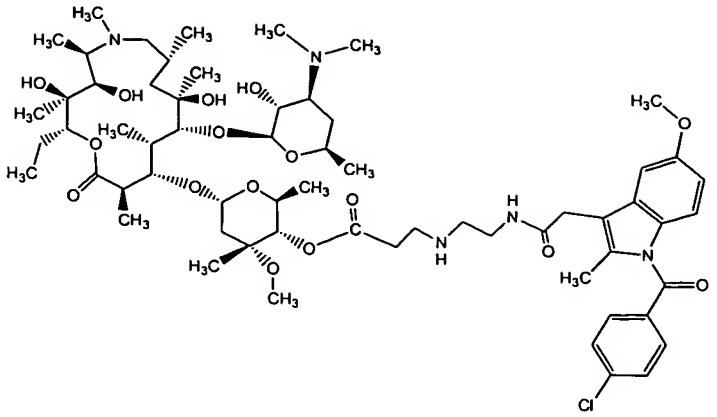

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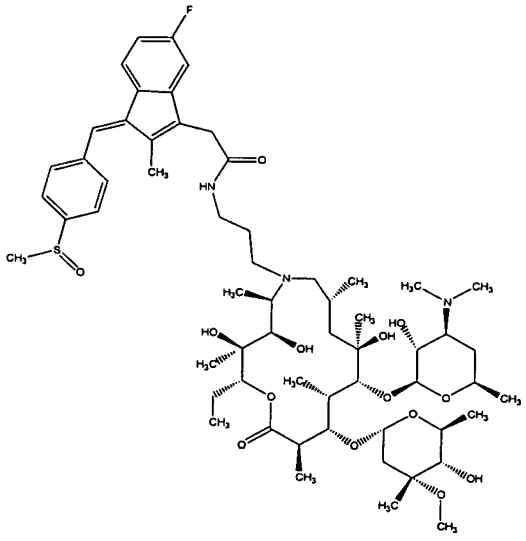

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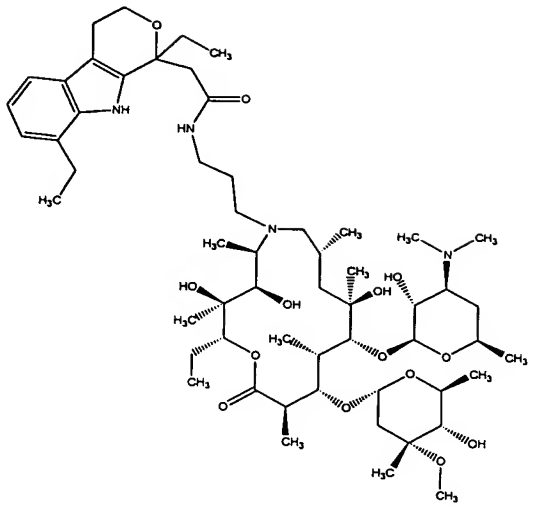

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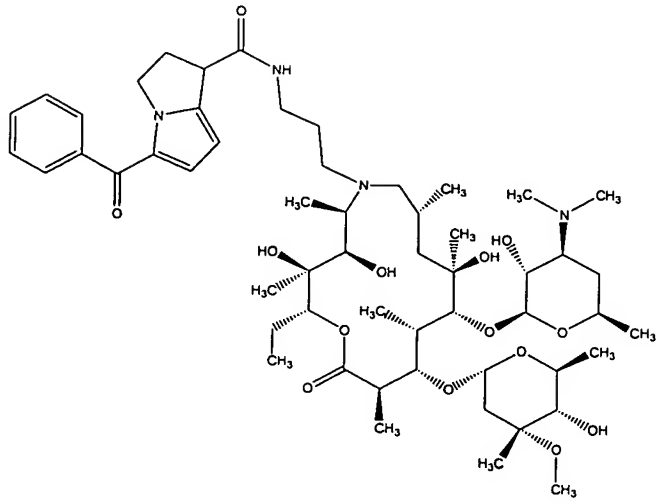

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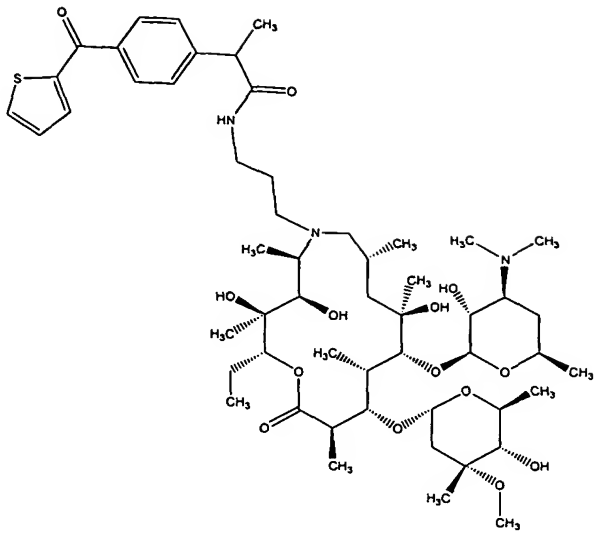

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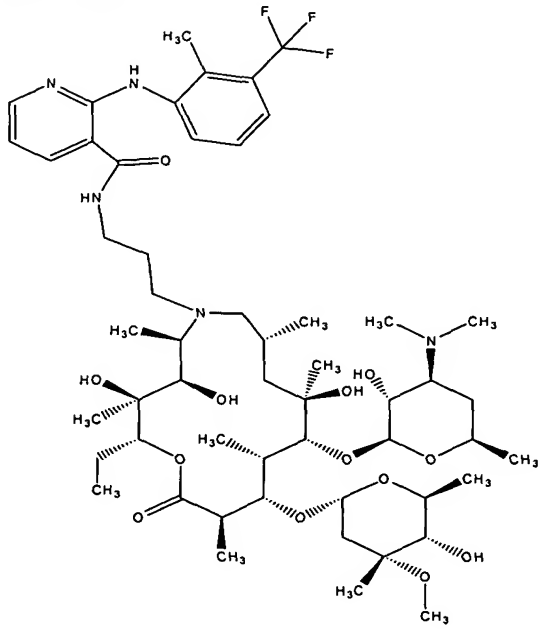

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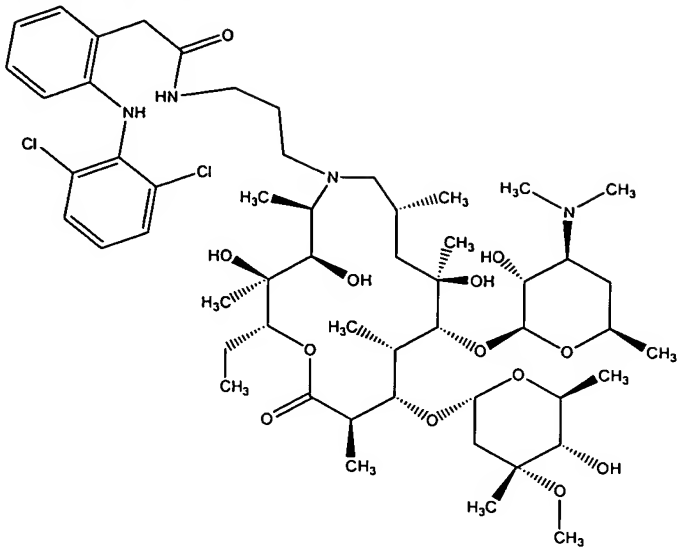

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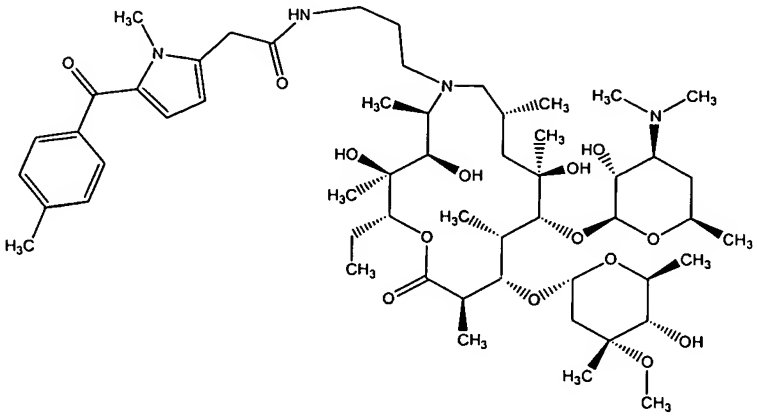
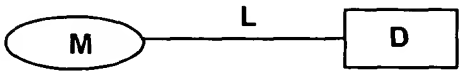


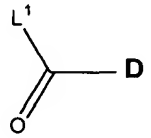
31. Process for the preparation a compound of Formula **I**



I

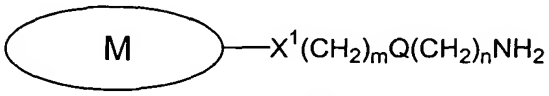
which comprises:

a) for a compound of Formula **I**, where X^2 is -NHC(O)-, by reacting a compound of Formula **V**:



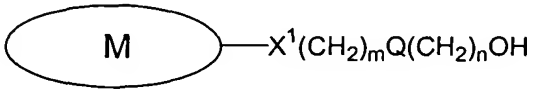
V

wherein L^1 represents a leaving group, and a free amino group of a macrolide represented by Formula **VIa**:



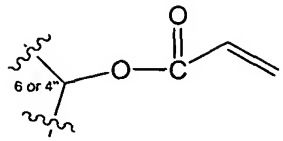
VIa

b) for a compound of Formula **I**, where X^2 is -OC(O)-, by reacting a compound of Formula **V** and the free hydroxyl group of a macrolide represented by Formula **VIb**:

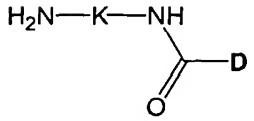


VIb

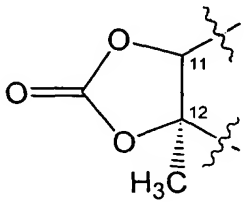
c) for a compound of Formula **I**, wherein X^1 is -OC(O)-, Q is -NH- and X^2 is -NHC(O)-, by reacting a macrolide represented by formula:



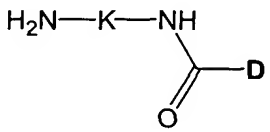
and a a free amino group of the compound represented by formula :



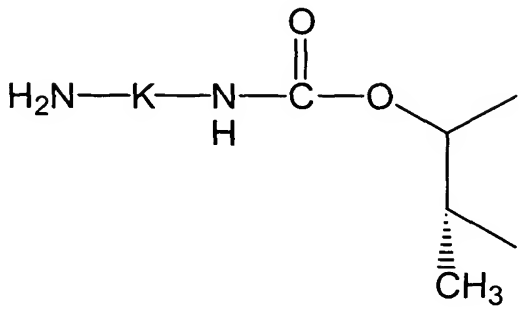
d) for a compound of Formula **I**, where X^1 is -OC(O)NH- and X^2 is -NHC(O)-, by reacting a macrolide represented by formula



and free amino group of of the compound represented by formula:



e) for a compound of Formula **I**, where X^1 is $-CH_2-$, Q is -NH- and X^2

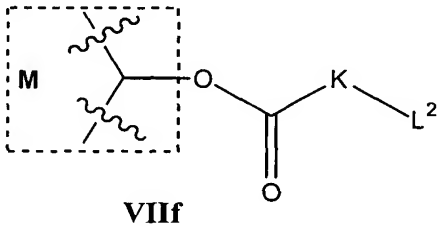


is

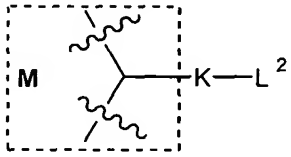
-NHC(O)-, by reacting a macrolide represented by formula:

and a compound of Formula **V**;

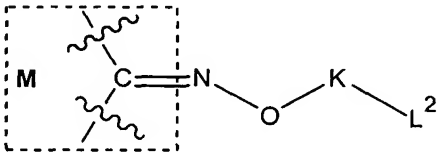
f) for a compound of Formula **I** by reacting a macrolide represented by Formula **VIIf** or by Formula **VIIg** or by Formula **VIIh** having a leaving group L^2



VIIf



VIIg



VIIh

with a free carboxylic acid of nonsteroidal anti-inflammatory subunit.

32. A pharmaceutical composition comprising a compound according to claim 1 and pharmaceutically acceptable salts or solvate thereof as well as pharmaceutically acceptable diluent or carrier.

33. A method of treating inflammatory diseases, disorders and conditions characterized by or associated with an undesirable inflammatory immune response, and all diseases and conditions induced by or associated with an excessive secretion of TNF-α and IL-1 which comprises administering to a subject a therapeutically effective amount of a compound according to claim 1.

34. A method of treating inflammatory conditions and immune or anaphylactic disorders associated with infiltration of leukocytes into inflamed tissue in a subject in need thereof which comprises administering to said subject a therapeutically effective amount of the compound represented by Formula **I** or a pharmaceutically acceptable salts or solvate thereof.

35. The method according to claim 34, wherein inflammatory conditions and immune disorders are selected from the group consisting of asthma, adult respiratory distress syndrome, bronchitis, and cystic fibrosis.

36. A method according to claim 34, wherein said inflammatory conditions and immune disorders are selected from the group consisting of inflammatory conditions or immune disorders of the lungs, joints, eyes, bowel, skin, and heart.

37. A method according to claim 34, wherein said inflammatory conditions and immune disorders are selected from the group consisting of asthma, adult respiratory distress syndrome, bronchitis, cystic fibrosis, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, uveitis, conjunctivitis,

inflammatory bowel conditions, Crohn's disease, ulcerative colitis, distal proctitis, psoriasis, eczema, dermatitis, coronary infarct damage, chronic inflammation, endotoxin shock, and smooth muscle proliferation disorders.

38. A method for abating inflamation in an affected organ or tissue comprising delivering to said organ or tissue a therapeutically effective amount of the compound represented by Formula I or a pharmaceutically acceptable salts or solvate thereof.